

CLAIMS:

1. An antibody to the human IL-12 p75 heterodimer which consists of a p35 subunit and a p40 subunit wherein said antibody

(a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and

(b) is produced from a mouse which is deficient in the gene encoding said p35 subunit or the p40 subunit of IL-12.

2. The antibody of claim 1, wherein the antibody is a monoclonal antibody.

3. The antibody of claim 1, wherein the antibody is produced from a cell line of the mouse.

4. The antibody of claim 1, wherein the antibody cross reacts with rhesus monkey IL-12.

5. The antibody of claim 1, wherein the antibody is humanized.

6. The antibody of claim 1, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12446, or a humanized antibody, thereof.

7. The antibody of claim 1, wherein the antibody is humanized.

6
B 8. The antibody of claim ~~1~~¹, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12447, *or a humanized antibody, thereof.*

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8. The antibody of claim ~~8~~⁶, wherein the antibody is humanized.

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B 8
B 10. The antibody of claim ~~1~~¹, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12448, *or a humanized antibody, thereof.*

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11. The antibody of claim ~~10~~⁸, wherein the antibody is humanized.

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B 12. The antibody of claim ~~1~~¹, wherein the antibody produced by a hybridoma having ATCC designation number HB-12449, *or a humanized antibody, thereof.*

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13. The antibody of claim ~~12~~¹⁰, wherein the antibody is humanized.

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14. A monoclonal antibody to human IL-12 which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer, wherein said monoclonal antibody

(a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and

(b) neutralizes at least about 90% of the bioactivity of human IL-12.

20
15. The antibody of claim 14, wherein the antibody neutralizes at least about 90% bioactivity of human IL-12 by inhibiting IL-12 stimulated PHA-activated human lymphoblast proliferation wherein

the concentration of said antibody is 0.5 µg/ml and the concentration of said human IL-12 is 0.25 ng/ml.

16. The antibody of claim 14, wherein the antibody neutralizes at least about 90% bioactivity of human IL-12 by inhibiting IL-12 stimulated IFN-γ production wherein the concentration of the antibody is 0.5 µg/ml and the concentration of said human IL-12 is 0.25 ng/ml.

17. The antibody of claim 14, wherein the antibody cross reacts with rhesus monkey IL-12.

18. The antibody of claim 14, wherein the antibody is humanized.

19. The antibody of claim 14, wherein the antibody is produced by a hybridoma.

20. The antibody of claim 19, wherein the antibody is humanized.

21. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12446, or a humanized antibody, thereof.

22. The antibody of claim 21, wherein the antibody is humanized.

23. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12447, or a humanized antibody, thereof.

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~~24.~~ The antibody of claim ¹⁴~~23~~, wherein the antibody is humanized.

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~~25.~~ The antibody of claim ²~~14~~, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12448, *or a humanized antibody thereof.*

⁵ ¹⁷
~~26.~~ The antibody of claim ¹⁶~~25~~, wherein the antibody is humanized.

^B ¹⁸
~~27.~~ The antibody of claim ²~~14~~, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12449, *or a humanized antibody thereof.*

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~~28.~~ The antibody of claim ¹⁷~~27~~, wherein the antibody is humanized.

²⁰ 29. A hybridoma that is capable of producing a monoclonal antibody to human IL-12 which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer, wherein said antibody

(a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and

b) is produced from a cell line obtained from a mouse deficient in a gene encoding said p35 subunit or said p40 subunit.

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~~30.~~ The hybridoma of claim ³~~29~~ wherein the hybridoma is HIL-12F3-5F2 having ATCC designation number HB-12446.

21

31.

The hybridoma of claim ~~29~~³ wherein the hybridoma is HIL-12F3-16F2 having ATCC designation number HB-12447.

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32.

The hybridoma of claim ~~29~~³, wherein the hybridoma is HIL-12F3-20E11 having ATCC designation number HB-12448.

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33.

The hybridoma of claim ~~29~~³, wherein the hybridoma is HIL-12F3-16G2 having ATCC designation number HB-12449.

34.

A method for producing an antibody that selectively immunologically reacts with the human IL-12 p75 heterodimer which consists of a p35 subunit and a p40 subunit, comprising the steps of:

- (a) immunizing a mammal deficient in a gene encoding said p35 subunit or said p40 subunit with the human IL-12 p75 heterodimer to produce antibodies;
- (b) obtaining antibodies from the immunized mammal;
- (c) screening said antibodies for their ability to selectively bind an epitope presented by the p75 heterodimer to obtain said selectively binding antibody.

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A method for producing a monoclonal antibody that selectively immunologically reacts with the human IL-12 p75 heterodimer which consists of a p35 subunit and a p40 subunit, comprising the steps of:

- (a) immunizing a mammal deficient in a gene encoding said p35 subunit or said p40 subunit with the human IL-12 p75 heterodimer to produce antibodies;
- (b) harvesting antibody producing cells from the immunized mammal;

43

